Electronically Mediated Selectivity in Ring Opening of 1-Azirines. The 3-*Z* Mode: Convenient Route to 2-Aza-1,3-dienes

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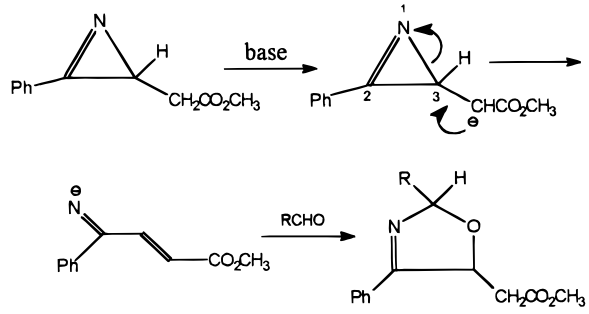
Reaction of 1-azirine-3-methylacrylates **1a**,**b** with imidazoles and pyrazoles under mild conditions results in the formation of 2-aza-1,3-dienes **2a**−**g** containing a potential leaving group at the 1-position. Simple alcohols (methanol and ethanol) react similarly with **1a**,**b** in the presence of sodium carbonate to afford **2h**−**j**. Utilization of **2** in the hetero Diels−Alder reaction with electron-deficient dienophiles is described.

Introduction

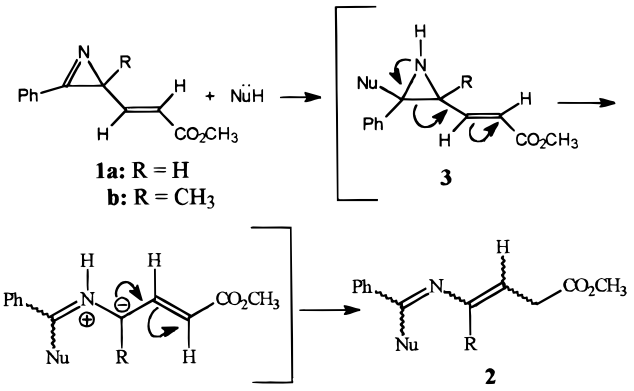
Recently, we reported a selective $N-C_3$ ring opening process in a 3-X substituted 1-azirine derived from a 3-acetate derivative (Scheme 1).[1] The interesting chemistry observed for 1-azirines containing the polyfunctional acrylate fragment at the 3-position[2] prompted us to utilize this electron-withdrawing substituent as a probe for a selective C_2-C_3 ring opening process (Scheme 2).

The success of this strategy evidently depends on the proper choice of nucleophiles for generation of the key aziridine intermediate. In this report, the results of our search for appropriate nucleophiles are presented, with special emphasis on synthetic and mechanistic implications.

Scheme 1



Scheme 2



Results and Discussion

Initially, a screening of nitrogen nucleophiles was performed. Although the more basic diethylamine reacted readily with 1-azirine-3-methyl acrylates **1a**,**b** (room temperature, 3 days) only to afford intractable material, the less basic *p*-toluidine did not react under these same conditions. Our search for a system of intermediate basicity led us to examine the behavior of imidazole in this reaction. ^{1}H NMR analysis of the crude product from a 2 day reaction of equimolar quantities of **1a** and imidazole (methylene chloride, room temperature) demonstrated the total consumption of reagents with formation of two new systems, one of which disappeared after an additional 5 days in solution. Purification of the final residue (column chromatography, Florisil) afforded 2-aza-1,3-diene **2a** in 45% yield, obtained as a 10:1 mixture of *Z*/*E* isomers[3] (Scheme 2 and Table 1).

The participation of a highly reactive aziridine intermediate **3** as the second system in the 2 day reaction is suggested by the presence of a methine hydrogen at δ 3.30 (d, $J = 7.5$ Hz) in the ^{1}H NMR spectrum of the crude reaction product. Purification of this material by column chromatography, in an attempt to isolate **3**, afforded only **2a** (30%). Reaction of the more hindered **1b** with imidazole proceeded more slowly (room temperature, 10 days) to eventually afford **2b** (60% yield). Interestingly, a NOE-difference experiment performed on **2b** revealed the predominance of the *E*-isomer (*Z*/*E* ratio of 1/12) (Figure 1).

The *s-cis* conformation is apparently favored for this isomer, as may be seen from the enrichment of an aromatic signal (either phenyl or imidazole) upon irradiation of the olefinic hydrogen. This situation may be contrasted with that of **2a** (Figure 2), wherein only irradiation of H_a produces this effect, thus indicating a preference for the *s-trans* conformation in **2a**. This

(1) Kascheres, A.; Sá, M. C. M. *J. Org. Chem.* **1996**, *61*, 3749.
(2) Kascheres, A.; Nunes da Silva, J., Jr.; Brandão, F. *Tetrahedron* **1997**, *53*, 7089.
(3) The existence of *syn*−*anti* isomerism is evident from the duplication of signals for both *Z* and *E* isomers in the ^{1}H NMR spectra of **2**. In the case of **2a**, the proportion for both *Z* and *E* isomers is approximately 10:1.

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Table 1. Reactions of 1-Azirine-3-methylacrylates 1a,b with Diazoles and Alcohols

	R	NüH	time (days)	product (% yield)	*Z*/*E* ratio[c]
1a	H	imidazole	7[a]	**2a** (45)	10:1
1b	CH_3	imidazole	10[a] or 3[b]	**2b** (60)	1:12[a] or 1:6[b,d]
1a	H	pyrazole	25[a]	**2c** (40)	10:1
1a	H	3,5-dimethylpyrazole	6[a] + 12 h[b] or 6[a,e]	**2d** (55) or (60)[e]	2.5:1
1a	H	2-ethylimidazole	10[a] + 2[b]	**2e** (61)	1.5:1
1b	CH_3	2-ethylimidazole	5[b]	**2f** (44)	1:1[d]
1b	CH_3	3,5-dimethylpyrazole	9[b,e]	**2g** (36)	2:1[d]
1a	H	methanol	1[a,e]	**2h** (75)	10:1
1b	CH_3	methanol	1[a,e]	**2i** (75)	1:2[d]
1a	H	ethanol	3[a,e]	**2j** (80)	10:1

[a] CH_2Cl_2 at room temperature. [b] C_6H_6 at 70 °C. [c] Proportion from the crude product. [d] Isomers were established through NOE-diff. [e] With added sodium carbonate.

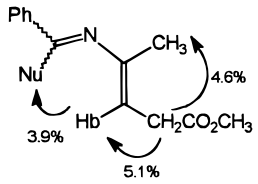


Figure 1. NOE-difference of 2-aza-1,3-diene **2b** (*E*).

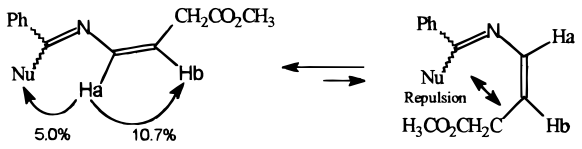
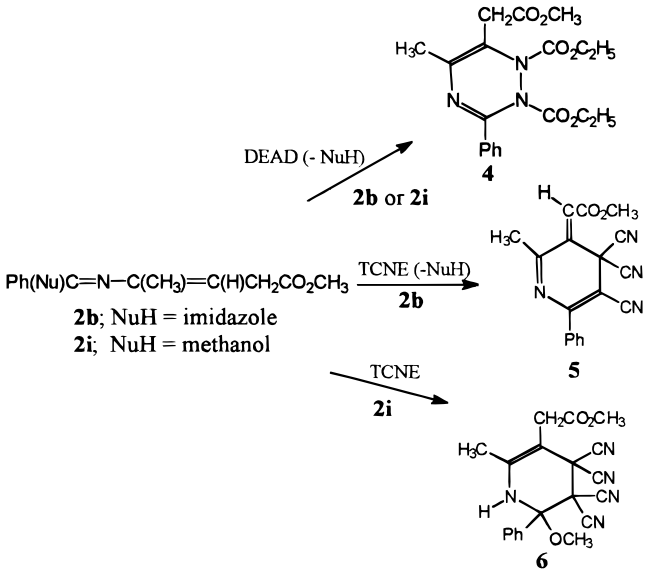


Figure 2. NOE-difference of 2-aza-1,3-diene **2a** (*Z*).

preference avoids an unfavorable interaction between Ph (or Nu) and the methyl acetate group.

A lower limit for diazole nucleophilicity necessary to the above process was established as being that of pyrazole, which reacted very slowly with **1a** (but not at all with **1b**) to eventually produce **2c** with the same *Z*/*E* ratio as that observed in **2a**. Interestingly, the more basic 3,5-dimethylpyrazole, although more reactive than pyrazole toward **1a** (but still unreactive toward **1b**), did not carry the process beyond the proposed aziridine stage at room temperature (6 days). Attempted isolation of this intermediate by column chromatography afforded only intractable material. An additional heating of the original reaction product in benzene (70 °C) was necessary to effect the transformation to **2d** with very low *Z*/*E* selectivity. This same situation prevailed in the reactions of **1a** and **1b** with 2-ethylimidazole, wherein additional heating was necessary to obtain **2e** and **2f**, respectively. Working on the hypothesis that ring opening of the aziridine intermediate should be base-catalyzed and that steric hindrance may slow this process, we decided to study the effect of adding a nonnucleophilic base to the medium. Thus, reaction of **1a** with 3,5-dimethylpyrazole in the presence of a catalytic amount of sodium carbonate afforded **2d** (60% yield) in the same conditions of 6 days at room temperature that produced only aziridine **3** in the absence of added base. Even reaction of **1b** with 3,5-dimethylpyrazole to produce **2g** (36% yield) could be achieved with added sodium carbonate, albeit requiring 9 days in benzene at 70 °C. This observation prompted us to examine the behavior of a weak oxygen-containing nucleophile in this reaction. Methanol was chosen as a model compound and, although no reaction with **1a** or **1b** occurred in the absence of base, a smooth transformation to **2h** and **2i** (1 day, 75% yields), respectively, was observed in the presence of sodium carbonate. Whereas

Scheme 3



1a reacted readily with ethanol under these conditions to afford **2j** (3 days, 80% yield), no reaction was observed with the more sterically hindered 2-propanol.

Cycloaddition Reactions of 2-Aza-1,3-dienes 2. The preparation and chemistry of 2-aza-1,3-dienes have received considerable attention in the recent literature.[4] Few synthetic routes to this system have been described, with the most important being acylation of iminoethers followed by allylation of the resulting acylimidates,[4a] intermolecular condensation of imines under acidic conditions,[4b] and an aza-Wittig reaction between *N*-vinylphosphazenes and carbonyl compounds.[4c] By far the most interesting aspect of their chemistry has been the construction of heterocycles through the use of the hetero Diels–Alder reaction.[4d] The azadienes **2** prepared in the present study range from electronically neutral (**2a**–**g**) to somewhat electron-donating (**2h**–**j**) and as such should react with electron-deficient dienophiles. Diethyl azodicarboxylate (DEAD) and tetracyanoethylene (TCNE) were thus chosen as potential partners for **2** in the hetero Diels–Alder process. Although **2a** did not react with DEAD or TCNE in benzene solution under reflux conditions (5 days), **2b** reacted readily at room temperature

(4) (a) Ghosez, L.; Bayard, Ph.; Nshimyumukiza, P.; Gouverneur, V.; Sainte, F.; Beaudegnies, R.; Rivera, M.; Frisque-Hesbain, A. M.; Wynants, C. *Tetrahedron* **1995**, *51*, 11021. (b) Barluenga, J.; Joglar, J.; González, F. J.; Fustero, S. *Synlett* **1990**, 129. (c) Palacios, F.; de Heredia, I. P.; Rubiales, G. *J. Org. Chem.* **1995**, *60*, 2384. (d) Boger, D. L. *Comprehensive Organic Synthesis*; Trost, B. M., Paquette, L. A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, p 451.

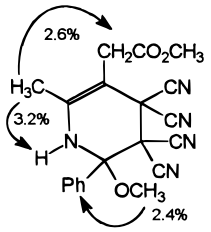


Figure 3. NOE-difference of tetrahydropyridine **6**.

(3 days) to afford cycloadducts **4**[5] (30% yield) and **5**[6] (40% yield), respectively (Scheme 3).

In both cases, the diazole nucleus serves as an efficient leaving group in the initial Diels−Alder adduct. This observation calls attention to this potentially valuable feature in the azadienes **2** prepared in the present study. We tentatively attribute the lack of reactivity of **2a** to the predominance of the *Z*-isomer, which does not readily assume the *s-cis* conformation necessary to the cycloaddition step. Interestingly, DEAD did react with azadienes **2** (R = H) that present lower *Z*/*E* ratios (i.e., **2d**) only to furnish complex mixtures. 1-Methoxy azadiene **2i** reacted with DEAD in a manner identical to that of **2b** to produce **4** through elimination of methanol from the initial cycloadduct. In contrast, reaction of **2i** with TCNE afforded cycloadduct **6** (80% yield) as the only product. A NOE-difference experiment performed on **6** (Figure 3) confirmed the sequence of substituents on the ring. Attempts to provoke elimination of methanol from **6** under mild basic conditions (Na_2CO_3, CH_2Cl_2, rt, 8 h) were unsuccessful. Electron-rich dienophiles (enamines and vinyl ethers) did not react with **2**.

Conclusions

The polyfunctional 1-azirine-3-methyl acrylates **1a**,**b** serve as valuable starting materials in a new approach to the aza-1,3-diene system. Reaction of **1a**,**b** with pyrazoles, imidazoles, and simple alcohols (under mild base-catalyzed conditions) affords derivatives **2** containing a potential leaving group at the 1-position. Attention is once again called to the versatility of 1-azirines containing higher order functionality at the 3-position. Azadienes **2** undergo the hetero Diels−Alder reaction with electron-deficient dienophiles.

Experimental Section

Materials and General Procedure. All chemicals were of reagent grade. DEAD was used after distillation under reduced pressure. TCNE was used after recrystallization from chlorobenzene. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded using TMS as internal reference. Melting points are uncorrected. Elemental analyses were performed by UNICAMP, Instituto de Química, Campinas, São Paulo, Brazil. Column chromatography utilized Florisil (Aldrich, 100−200 mesh particle size). 1-Azirines **1a**,**b** were prepared according to the described method.[7,8] NMR data for compounds **2a**−**j** correspond to the major *syn-anti* isomer.

General Procedure for Reactions of 1-Azirines 1 with Diazoles. A solution containing **1** and diazole in methylene chloride was allowed to stand at room temperature (method A), or a solution in benzene was maintained at 70 °C (method B). After evaporation of the solvent, the resulting yellow oils were submitted to column chromatography to afford **2** as pale yellow oils. The following azadienes **2** were obtained.

Methyl 6-(1*H*-imidazolyl)-6-phenyl-3,5-azahexadienoate 2a was obtained as a 10:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1a** (92 mg, 0.46 mmol) and imidazole (31 mg, 0.46 mmol) in CH_2Cl_2 (5 mL) using method A (7 d, 56 mg, 45% yield). PhH−Et_2O (85:15) was used as eluent. **2a** (*Z*): IR (film) 1735, 1618 cm^{-1}; ^{1}H NMR (CCl_4) δ 3.48 (dd, J = 1.4, 7.0 Hz, 2 H), 3.66 (s, 3 H), 5.43 (q, J = 7.0 Hz, 1 H), 6.53 (dt, J = 1.4, 7.0 Hz, 1 H), 6.94 (s, 1 H), 7.38−7.58 (m, 7 H); ^{13}C NMR δ 31.5, 51.0, 116.8, 121.6, 128.9−130.6, 134.0, 136.5, 150.3, 170.2. **2a** (*E*): ^{1}H NMR[9] (CCl_4) δ 3.00 (d, J = 7.6 Hz, 2 H), 3.63 (s, 3 H), 6.04 (m, 1 H); ^{13}C NMR[9] δ 35.1, 51.1, 116.6, 123.6, 150.0, 169.5. Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.89; H, 5.62; N, 15.61. Found: C, 66.77; H, 5.83; N, 15.48.

Methyl 6-(1*H*-imidazolyl)-4-methyl-6-phenyl-3,5-azahexadienoate 2b was obtained as a 1:6 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1b** (118 mg, 0.55 mmol) and imidazole (38 mg, 0.55 mmol) in C_6H_6 (6 mL) using method B (3 d, 100 mg, 60% yield). PhH−Et_2O (80:20) was used as eluent. **2b** (*E*): IR (film) 1737, 1652 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.66 (s, 3 H), 2.81 (d, J = 7.7 Hz, 2 H), 3.51 (s, 3 H), 4.66 (t, J = 7.7 Hz, 1 H), 6.93 (s, 1 H), 7.31−7.53 (m, 7 H); ^{13}C NMR δ 16.7, 32.5, 51.0, 106.2, 116.9, 128.4−130.1, 131.3, 136.6, 143.3, 149.4, 170.3. **2b** (*Z*): ^{1}H NMR[9] (CCl_4) δ 1.56 (s, 3 H), 2.92 (d, J = 7.0 Hz, 2 H), 3.58 (s, 3 H), 4.75 (t, J = 7.0 Hz, 1 H), 6.96 (s, 1 H). Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{16}H_{17}N_3O_2$: C, 67.81; H, 6.05; N, 14.84. Found: C, 67.98; H, 6.17; N, 14.61.

Methyl 6-phenyl-6-(1*H*-pyrazolyl)-3,5-azahexadienoate 2c was obtained as a 15:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1a** (53 mg, 0.27 mmol) and pyrazole (18 mg, 0.27 mmol) in CH_2Cl_2 (5 mL) using method A (25 d, 29 mg, 40% yield). PhH−Et_2O (90:10) was used as eluent. **2c** (*Z*): IR (film) 1737, 1618 cm^{-1}; ^{1}H NMR (CCl_4) δ 3.49 (dd, J = 1.6, 7.1 Hz, 2 H), 3.65 (s, 3 H), 5.39 (q, J = 7.1 Hz, 1 H), 6.36 (s, 1 H), 6.63 (dt, J = 1.6, 7.1 Hz, 1 H), 7.29−7.47 (m, 6 H), 8.49 (s, 1 H); ^{13}C NMR δ 31.5, 51.0, 107.5, 120.2, 127.4−129.6, 130.0, 134.3, 141.6, 153.5, 170.4. **2c** (*E*): ^{1}H NMR[9] (CCl_4) δ 3.00 (d, J = 7.5 Hz, 2 H). Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.89; H, 5.62, N, 15.61. Found: C, 66.87; H, 5.51; N, 15.41.

Methyl 6-(1*H*-3,5-dimethylpyrazolyl)-6-phenyl-3,5-azahexadienoate 2d was obtained as a 2.5:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1a** (165 mg, 0.82 mmol) and 3,5-dimethylpyrazole (78 mg, 0.82 mmol) in CH_2Cl_2 (7 mL) using method A (6 d) plus method B (12 h) in C_6H_6 (7 mL) (134 mg, 55% yield). PhH−Et_2O (95:5) was used as eluent. **2d** (*Z*): IR (film) 1738, 1645 cm^{-1}; ^{1}H NMR (CCl_4) δ 2.03 (s, 3 H), 2.24 (s, 3 H), 3.63 (dd, J = 1.6, 7.2 Hz, 2 H), 3.65 (s, 3 H), 6.43 (dt, J = 1.6, 7.3 Hz, 1 H), 5.64 (dt, J = 7.2, 7.3 Hz, 1 H), 5.87 (s, 1 H), 7.20−7.52 (m, 5 H); ^{13}C NMR δ 10.8, 13.4, 31.8, 51.0, 105.2, 124.5, 128.0−129.2, 134.4, 135.0, 140.1, 148.8, 149.0, 170.2. **2d** (*E*): IR (film) 1738, 1645 cm^{-1}; ^{1}H NMR (CCl_4) δ 2.03 (s, 3 H), 2.26 (s, 3 H), 3.11 (dd, J = 1.6, 7.4 Hz, 2 H), 3.64 (s, 3 H), 5.88 (s, 1 H), 6.26 (dt, J = 7.4, 13.2 Hz, 1 H), 6.42 (dt, J = 1.6, 13.2 Hz, 1 H), 7.20−7.49 (m, 8 H); ^{13}C NMR δ 10.8, 13.5, 35.4, 51.2, 105.3, 127.1, 128.1−130.9, 135.2, 137.1, 140.3, 148.7, 149.2, 169.8. Elemental analysis was

(5) To the best of our knowledge, the only other example of a 1,2-dihydro-1,2,4-triazine is that observed upon electrolytic reduction of a simple aromatic nucleus: Pinson, J.; M'Packo, J.-P.; Vinot, N.; Armand, J.; Bassinet, P. *Can. J. Chem.* **1972**, *50*, 1581. An interesting feature in the ^{1}H NMR spectrum of **4** is the presence of diastereotopic methylene hydrogens, thus demonstrating the nonplanar nature of this potentially 8π electron system.

(6) The geometry of the *exo* double bond in **5** was established through a NOE-difference experiment [irradiation of the imino methyl produced an enrichment of the olefinic hydrogen (8.3%)].

(7) Padwa, A.; Smolanoff, J.; Tremper, A. *J. Am. Chem. Soc.* **1975**, *6*, 4682.

(8) Kascheres, A.; Oliveira, C. M. A.; de Azevedo, M. B. M.; Nobre, C. M. S. *J. Org. Chem.* **1991**, 56, 7.

(9) Partial data. Some signals here are hidden within the signals of the major isomer.

obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{17}H_{19}N_3O_2$: C, 68.65; H, 6.44; N, 14.14. Found: C, 68.51; H, 6.66; N, 14.01.

Methyl 6-(1*H*-2-ethylimidazolyl)-6-phenyl-3,5-azahexadienoate 2e was obtained as a 1.5:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1a** (63 mg, 0.32 mmol) and 2-ethylimidazole (30 mg, 0.32 mmol) in CH_2Cl_2 (4 mL) using method A (10 d) plus method B (2 d) in C_6H_6 (4 mL) (57 mg, 60% yield). PhH−Et_2O (70:30) was used as eluent. **2e** (*Z*): IR (film) 1738, 1571 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.19 (t, J = 7.6 Hz, 3 H), 2.39 (q, J = 7.6 Hz, 2 H), 3.62 (dd, J = 1.6, 7.2 Hz, 2 H), 3.68 (s, 3 H), 5.72 (q, J = 7.2 Hz, 1 H), 6.43 (dt, J = 1.6, 7.2 Hz, 1 H), 6.78 (s, 1 H), 6.99 (s, 1 H), 7.35−7.56 (m, 5 H); ^{13}C NMR δ 12.0, 20.4, 31.8, 51.1, 117.7, 125.8, 128.1−128.5, 131.4, 133.6, 134.6, 147.0, 169.8. **2e** (*E*): IR (film) 1738, 1571 cm^{-1}; ^{1}H NMR[9] (CCl_4) δ 1.19 (t, J = 7.6 Hz, 3 H), 2.39 (q, J = 7.6 Hz, 2 H), 3.11 (dd, J = 1.5, 6.0 Hz, 2 H), 3.66 (s, 3 H), 6.36 (dt, J = 6.0, 13.0 Hz, 1 H), 6.44 (dt, J = 1.5, 13.0 Hz, 1 H), 6.78 (s, 1 H), 7.00 (s, 1 H). Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{17}H_{19}N_3O_2$: C, 68.65; H, 6.44; N, 14.14. Found: C, 68.83; H, 6.31; N, 13.96.

Methyl 6-(1*H*-2-ethylimidazolyl)-4-methyl-6-phenyl-3,5-azahexadienoate 2f was obtained as a 1:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1b** (52 mg, 0.25 mmol) and 2-ethylimidazole (23 mg, 0.25 mmol) in C_6H_6 (4 mL) using method B (5 d, 33 mg, 44% yield). PhH−Et_2O (60:40) was used as eluent. **2f** (*Z*): IR (film) 1735, 1637 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.17 (t, J = 7.5 Hz, 3 H), 1.40 (s, 3 H), 2.31 (q, J = 7.5 Hz, 2 H), 3.16 (d, J = 7.0 Hz, 2 H), 3.60 (s, 3 H), 5.09 (t, J = 7.0 Hz, 1 H), 6.93 (s, 1 H), 6.98 (s, 1 H), 7.36−7.55 (m, 5 H); ^{13}C NMR δ 11.8, 19.2, 21.0, 32.5, 51.0, 113.6, 118.6, 128.4−128.5, 131.6, 135.4, 142.4, 147.4, 148.6, 170.9. **2f** (*E*): IR (film) 1735, 1637 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.19 (t, J = 7.5 Hz, 3 H), 1.62 (s, 3 H), 2.37 (q, J = 7.5 Hz, 2 H), 2.93 (d, J = 7.7 Hz, 2 H), 3.61 (s, 3 H), 4.96 (t, J = 7.7 Hz, 1 H), 6.77 (s, 1 H), 6.91 (s, 1 H), 7.32−7.52 (m, 5 H); ^{13}C NMR δ 11.8, 15.4, 20.7, 32.6, 51.1, 109.0, 118.1, 128.1−128.2, 131.3, 134.9, 143.2, 146.7, 148.5, 169.8. Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{18}H_{21}N_3O_2$: C, 69.42; H, 6.80; N, 13.50. Found: C, 69.58; H, 6.51; N, 13.31.

Methyl 6-(1*H*-3,5-dimethylpyrazolyl)-4-methyl-6-phenyl-3,5-azahexadienoate 2g was obtained as a 2:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1b** (57 mg, 0.27 mmol) and 3,5-dimethylpyrazole (26 mg, 0.27 mmol) in C_6H_6 (7 mL) using Na_2CO_3 (11 mg, 0.11 mmol) as catalyst through method B (9 d, 31 mg, 36% yield). PhH−Et_2O (85:15) was used as eluent. **2g** (*Z*): IR (film) 1737, 1646 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.60 (s, 3 H), 2.10 (s, 3H), 2.58 (s, 3 H), 2.87 (d, J = 7.0 Hz, 2 H), 3.66 (s, 3 H), 4.67 (t, J = 7.0 Hz, 1 H), 5.87 (s, 1 H), 7.27−7.49 (m, 5 H); ^{13}C NMR δ 11.2, 13.8, 22.0, 32.8, 51.9, 104.1, 128.6−129.3, 130.8, 133.7, 143.4, 150.1, 173.0. **2g** (*E*): IR (film) 1737, 1646 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.65 (s, 3 H), 2.05 (s, 3H), 2.21 (s, 3 H), 2.92 (d, J = 7.3 Hz, 2 H), 3.59 (s, 3 H), 4.88 (t, J = 7.3 Hz, 1 H), 5.79 (s, 1 H), 7.22−7.49 (m, 5 H); ^{13}C NMR δ 13.9, 14.1, 16.0, 33.6, 52.2, 109.9, 129.0−129.6, 132.0, 135.9, 141.7, 150.3, 172.7. Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{18}H_{21}N_3O_2$: C, 69.42; H, 6.80; N, 13.50. Found: C, 69.14; H, 6.51; N, 13.74.

General Procedure for Reactions of 1-Azirines 1 with Alcohols. A suspension containing **1** and Na_2CO_3 (one-third equiv) as catalyst in methanol or ethanol was allowed to stand at room temperature with vigorous magnetic stirring. After evaporation of the alcohol, the resulting mixture was washed with distilled water followed by extraction with methylene chloride. The organic layer was dried (magnesium sulfate) and stripped of solvent to afford **2** as pale yellow oils. The following azadienes **2** were obtained.

Methyl 6-methoxy-6-phenyl-3,5-azahexadienoate 2h was obtained as a 10:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1a** (38 mg, 0.19 mmol) and methanol (5 mL) (1 d, 34 mg, 75% yield). **2h** (*Z*): IR (film) 1738, 1633 cm^{-1}; ^{1}H NMR (CCl_4) δ 3.37 (dd, J = 1.6, 7.1 Hz, 2 H), 3.63 (s, 3 H), 3.87 (s, 3 H), 5.10 (q, J = 7.1 Hz, 1 H), 6.58 (dt, J = 1.6, 7.1 Hz, 1 H), 7.35−7.45 (m, 5 H); ^{13}C NMR δ 31.2, 50.8, 53.1, 114.1, 127.8−129.7, 134.2, 160.9, 170.8. **2h** (*E*): ^{1}H NMR[9] (CCl_4) δ 2.95 (d, J = 6.9 Hz, 2 H), 3.62 (s, 3 H), 3.83 (s, 3 H), 5.63 (m, 1 H). Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.81; H, 6.59; N, 6.23.

Methyl 6-methoxy-4-methyl-6-phenyl-3,5-azahexadienoate 2i was obtained as a 1:2 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1b** (60 mg, 0.28 mmol) and methanol (7 mL) (1 d, 54 mg, 75% yield). **2i** (*Z*): IR (film) 1735, 1630 cm^{-1}; ^{1}H NMR[9] (CCl_4) δ 1.68 (s, 3 H), 2.86 (d, J = 7.5 Hz, 2 H), 3.52 (s, 3 H), 3.77 (s, 3 H), 4.68 (t, J = 7.5 Hz, 1 H); ^{13}C NMR[9] δ 22.0, 32.0, 50.7, 53.0, 102.8, 142.1, 156.1, 171.0. **2i** (*E*): IR (film) 1735, 1630 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.70 (s, 3 H), 2.86 (d, J = 7.5 Hz, 2 H), 3.53 (s, 3 H), 3.77 (s, 3 H), 4.57 (t, J = 7.5 Hz, 1 H), 7.25−7.60 (m, 5 H); ^{13}C NMR δ 17.2, 32.8, 50.8, 53.0, 103.5, 127.5−127.8, 143.6, 156.6, 170.6. Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.81; N, 5.57.

Methyl 6-ethoxy-6-phenyl-3,5-azahexadienoate 2j was obtained as a 10:1 mixture of *Z*:*E* diastereomers (based on ^{1}H NMR) from the reaction of azirine **1a** (28 mg, 0.14 mmol) and ethanol (4 mL) (3 d, 29 mg, 80% yield). **2j** (*Z*): IR (film) 1739, 1630 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.38 (t, J = 7.1 Hz, 3 H), 3.34 (d, J = 7.0 Hz, 2 H), 3.63 (s, 3 H), 4.32 (q, J = 7.1 Hz, 2 H), 5.07 (m, 1 H), 6.57 (d, J = 7.0 Hz, 1 H), 7.34−7.43 (m, 5 H);^{13}C NMR δ 14.2, 31.2, 50.8, 61.4, 113.8, 127.7−129.5, 134.4, 160.5, 170.8. **2j** (*E*): ^{1}H NMR[9] (CCl_4) δ 1.25 (t, J = 7.0 Hz, 3 H), 2.93 (d, J = 7.0 Hz, 2 H), 3.62 (s, 3 H), 4.08 (q, J = 7.0 Hz, 2 H), 5.55 (m, 1 H), 6.82 (d, J = 13.0 Hz, 1 H). Elemental analysis was obtained for the *Z*:*E* mixture. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.87; H, 6.85; N, 5.78.

Methyl-1,2-bis(ethoxycarbonyl)-5-methyl-3-phenyl-1,2-dihydro-1,2,4-triazine-6-acetate 4. A solution containing **2b** (142 mg, 0.50 mmol) and diethyl azodicarboxylate (87 mg, 0.50 mmol) in benzene (8 mL) was allowed to stand at room temperature for 3 days. After evaporation of the solvent, the resulting yelow oil was submitted to column chromatography using PhH−Et_2O (95:5) as eluent to afford 1,2-dihydro-1,2,4-triazine **4** (58 mg, 0.15 mmol, 30% yield). An analytical sample was obtained by trituration with petroleum ether to afford a colorless solid: mp 96−97 °C; IR (KBr) 1734, 1636, 1565 cm^{-1}; ^{1}H NMR (CCl_4, 333 °K) δ 1.10 (t, J = 7.1 Hz, 3 H), 1.31 (t, J = 7.1 Hz, 3 H), 2.05 (s, 3 H), 3.35 (d, J = 16.6 Hz, 1 H), 3.65 (s, 3 H), 3.73 (d, J = 16.6 Hz, 1 H), 4.08 (m, 2 H), 4.22 (m, 2 H), 7.34 (m, 3 H), 7.91 (dd, J = 1.5, 4.6 Hz, 2 H); ^{13}C NMR δ 13.9, 14.2, 16.5, 35.0, 51.2, 62.2, 127.5, 128.4, 130.3, 133.8, 134.5, 152.0, 153.8, 168.3; MS *m*/*z* 389 (M^+, 8.4), 244 (100). Anal. Calcd for $C_{19}H_{23}N_3O_6$: C, 58.59; H, 5.96; N, 10.79. Found: C, 58.94; H, 5.60; N, 10.65.

3-Carbomethoxymethylene-4,4,5-tricyane-2-methyl-6-phenyl-3,4-dihydropyridine 5. A solution containing **2b** (89 mg, 0.31 mmol) and tetracyanoethylene (40 mg, 0.31 mmol) in methylene chloride (7 mL) was allowed to stand at room temperature for 1 h. After evaporation of the solvent, the resulting dark brown oil was submitted to column chromatography using CH_2Cl_2−Et_2O (82:18) as eluent to afford dihydropyridine **5** (39 mg, 0.12 mmol, 40% yield). An analytical sample was obtained by trituration with a mixture of CH_2Cl_2 and petroleum ether (50:50) to afford a pale yellow solid: mp 169−173 °C; IR (KBr) 1736, 1607, 1513 cm^{-1}; ^{1}H NMR (CD_3CN) δ 2.05 (s, 3 H), 3.92 (s, 3 H), 6.78 (s, 1 H), 7.58−7.66 (m, 5 H); ^{13}C NMR δ 23.4, 52.5, 53.5, 112.5−113.0, 128.3, 129.5−133.2, 131.7, 132.0, 135.7, 158.8, 164.6; MS *m*/*z* 316 (M^+, 95.8). Anal. Calcd for $C_{18}H_{12}N_4O_2 \cdot H_2O$: C, 64.65; H, 4.22; N, 16.76. Found: C, 64.94; H, 3.94; N, 17.02.

Methyl-4,4,5,5-tetracyane-6-methoxy-2-methyl-6-phenyl-1,4,5,6-tetrahydropyridine-3-acetate 6. A solution containing **2i** (66 mg, 0.27 mmol) and tetracyanoethylene (34 mg, 0.27 mmol) in methylene chloride (4 mL) was allowed to stand at room temperature for 1 h. After evaporation of the solvent, the resulting dark brown oil was submitted to column chromatography using CH_2Cl_2−Et_2O (95:5) as eluent to afford tetrahydropyridine **6** (81 mg, 0.21 mmol, 80% yield) as a pale yellow oil: IR (film) 1741, 1668, 1489 cm^{-1}; ^{1}H NMR (CCl_4) δ

2.09 (s, 3 H), 3.23 (s, 3 H), 3.40 (s, 2 H), 3.77 (s, 3 H), 5.23 (s, 1 H), 7.55−7.75 (m, 5 H); ^{13}C NMR δ 18.4, 34.4, 43.5, 49.9, 52.6, 109.4−111.4, 127.9−131.9, 131.1, 140.2, 169.9. Anal. Calcd for $C_{20}H_{17}N_5O_3$: C, 63.98; H, 4.57; N, 18.66. Found: C, 63.74; H, 4.71; N, 18.8.

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Supporting Information Available: NOE-difference of **2f**, **2i**, **2g**, and **5** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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